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MESTRADO INTEGRADO EM MEDICINA

Clínica Universitária de Neurologia

Papel da Fibrilhação Auricular no Jovem com Acidente Vascular Isquémico

Cláudia Filipa Antunes Pereira Dias Ribeiro

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Orientado por:

Prof. Dra. Ana Catarina Fonseca

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ABSTRACT

Atrial Fibrillation (AF) is a cause of cardioembolic stroke and therefore an important finding in the etiological investigation of ischemic stroke (IS). Currently etiological investigation for IS includes the performance of an Electrocardiogram (EKG) and a 24hour-EKG monitoring to detect AF in all stroke patients independently of their age. However it is known that AF is a disease mainly of older individuals. The aim of this work was to study the prevalence of *de novo* AF as a cause of stroke among a sample of Portuguese patients aged 18 to 50 years old admitted to a stroke unit and to perform a systematic literature review and meta-analysis to estimate the prevalence of atrial fibrillation as a cause of stroke in young stroke patients.

We did a single-centre observational retrospective analysis. All the data was collected from the database of the department of neurology of the Hospital de Santa Maria (HSM) from 1st January of 2013 until 31st December of 2015. We found a zero prevalence of AF 0,015% 95 Confidence Interval (CI) (0,00 – 0,055%) . In the meta-analysis we found a pooled prevalence of atrial fibrillation as a cause of stroke in young adults of 0.034% 95 CI (0.022-0.045) These findings are important to reconsider the performance of a 24-h EKG in all young patients.

Key Words: Young; Fibrillation; Cryptogenic Stroke; Holter monitoring,

The present dissertation is based on the author´s opinion and not the FML´s.

RESUMO

A Fibrilhação Auricular (FA) é uma causa cardíaca de acidente vascular e consequentemente um achado importante na investigação etiológica de acidente vascular isquémico (AVCI). A investigação da etiologia do AVCI inclui a realização de um eletrocardiograma (ECG) e uma monitorização electrocardiografica cardiaca de 24horas para deteção de FA em todos os doentes, independentemente da sua idade. Contudo, é sabido que a FA é uma doença mais prevalente em indivíduos com mais de cinquenta anos. O objetivo deste trabalho foi estudar a prevalência de FA, como uma causa de AVC, numa amostra da população Portuguesa, com idades entre os 18 a 50 anos, admitidos numa unidade de AVC, e, realizar uma revisão sistemática e meta-análise para determinar a prevalência da FA como causa de AVC isquémico nos doentes jovens.

Realizámos uma análise observacional retrospetiva de centro-único. Todos os dados foram recolhidos da base de dados do departamento de neurologia do Hospital de Santa Maria (HSM) desde 1 de Janeiro de 2013 até 31 de Dezembro de 2015.

A prevalência de FA encontrada, foi de zero, com um intervalo de confiança entre 0 e 0.055%. Na nossa meta-análise encontrou uma prevalência da FA, como causa de AVCI nos jovens adultos de 0 e 0.055%. A meta-analise, revelou uma prevalência agrupada de FA como causa de AVC, nos adultos jovens, de 0.034% 95CI (0.022-0.045) Estes achados são importantes, para que se reconsidere a necessidade de realizar 24h-ECG em todos os doentes jovens.

Palavras-chave: jovens; Fibrilhação; AVC indeterminado; Holter.

O trabalho final exprime a opinião do autor e não da FML.

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INTRODUCTION

Stroke is a cause of high morbidity and mortality worldwide[1]. Finding a cause of stroke is a daily challenge to the trained neurologist, who has to treat young adults with ischemic stroke.[2]

Causes of stroke in young adults differ from the ones found in older patients. Young adults tend to have more frequently etiologies such as: arterial dissections, cardioembolism related to Patent Foramen Ovale; vasculitis or hematologic disorders[3]. In older patients the main causes of ischemic stroke are atrial fibrillation or large vessel disease. Young adults tend to have a lower frequency of conventional cardiovascular risk factors (i.e. hypertension, dyslipidaemia, diabetes mellitus) than older patients [4][5] that partly explains the different etiologies that may be found.

Atrial Fibrillation is a common sustained arrhythmia with an estimated prevalence of six million in Europe and these numbers are expected to double in the next 50 years. It confers a 5 fold increase risk of stroke, being responsible for one in five ischaemic strokes, which are often fatal. Those patients who survive are left more disabled and more likely to suffer a recurrence of their stroke, when compared to other causes of stroke, and its likelihood increases with age. AF is defined as a cardiac arrhythmia with the following characteristics:

- The surface EKG shows 'absolutely' irregular RR intervals;
- There are no distinct P waves on the surface EKG. Some apparently regular atrial electrical activity may be seen in some EKG leads, most often in lead V1.
- The atrial cycle length (when visible) is usually variable and 200 ms (300 bpm).

Clinically, we can distinguish five types of AF based on the presentation and duration of the arrhythmia: first diagnosed, paroxysmal, persistent, long-standing persistent, and permanent AF.

1. First diagnosed - Every patient who presents with AF for the first time, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms.
2. Paroxysmal AF - is self-terminating, usually within 48h. Although AF paroxysms may continue for up to 7 days, the 48h time point is clinically important, because after this the likelihood of spontaneous conversion is low.

3. Persistent AF - when an AF episode either lasts longer than 7 days or requires termination by cardioversion.
4. Long-standing persistent AF - AF lasted for ≥1 year when it is decided to adopt a rhythm control strategy.
5. Permanent AF - when the presence of the arrhythmia is accepted by the patient (and physician). [13]

Atrial Fibrillation occurs due to abnormalities in the atrial tissue. This can be structural in the setting of underlying heart disease associated with: hypertension, coronary artery disease, valvular heart disease. Atrial tissue promotes abnormal impulse formation and/or propagation. In AF, ischaemic stroke and systemic arterial embolism are generally explained with thrombus originating from left atrial appendage. [11] AF affects calcium homeostasis. With an alteration in the physiologic calcium homeostasis, AF induces further electrophysiological changes in the atria. This process leads to shortening of the atrial effective refractory period, as well as atrial dilation, stretch and fibrosis.[12]

In one third of young adults who suffer an ischemic stroke (IS) the cause is unknown [14]. Both, the European Stroke organization and the American Heart Association/ American Stroke Association guidelines, suggest performing an EKG and at least a 24 hours Holter monitoring (24h-HM), or continuous monitoring, to detect AF on all patients; and on a selected number of patients, who presents with IS[15],[16]. Several studies report the benefit of using Holter Monitoring (HM) in order to detect AF.[17],[7],[18],[19],[20],[21],[22],[23],[24],[25],[26] Most of the analysed data shows a low prevalence of atrial fibrillation in young adults.. [6],[7],[8],[9]. The FAMA study (a cross-sectional study of a representative sample of the Portuguese population aged 40 and over, resident in Portugal, which aimed to determine the prevalence and incidence of AF), reports a prevalence of 0,2% of AF in patients under 50 years old, with a total prevalence of 2,5%.[10]

In this paper we aim to analyse the prevalence of *de novo* AF in young stroke patients as a cause of Cryptogenic Ischemic Stroke (CIS).

SUBJECTS AND METHODS

In order to determine the prevalence of atrial fibrillation as a cause of stroke among young adults we performed a systematic review of the literature and a retrospective analysis, of a case series of patients, admitted to the stroke unit of a university hospital.

PUBMED was systematically searched using the following keywords: stroke AND young AND (atrial fibrillation [Mesh] OR Holter OR electrocardiogram OR arrhythmia). We selected studies, from 1998 until 2015 (last search was made on 1st January 2016), performed on subjects aged under 50 years old with an acute brain infarction from cryptogenic origin (to whom an EKG was performed). Articles had to be written in English, Portuguese, Spanish, Italian or French language. We excluded case-controls, author´s opinion, case-reports, clinical comments, letters, and editorials.
The following data was recorded in each study: Total number of young stroke patients included; Percentage of patients studied with EKG and 24 hours Holter monitoring (24h-HM).

This systematic review followed by the Meta-analysis of Observational Studies in Epidemiology guidelines for reporting Meta-Analyses and Systematic Reviews of Observational Studies.

This is a single-centre observational retrospective analysis, taken place at Hospital of Santa Maria, department of Neurology, Lisbon (Portugal). Hospital de Santa Maria is a tertiary stroke centre in Portugal, which serves directly a population of 372831, although this number may be underestimated, because patients from primary or secondary Hospitals can be transferred to here.

We analysed data collected into the Hospital´s database from patients with an acute IS aged between 18 and 50 years old, admitted from the Emergency Room (ER) to the Neurology department (ND) from 1st January 2013 to 31st December 2015.

In the ER all patients underwent a 1) Brain CT; 2) serial laboratory samples containing: hematologic evaluation; biochemistry; syphilis serology; auto-antibodies searched on plasma; pro-thrombotic states; urinalysis 3) admission ECG; in the ND: 1) Ultrasound of cervical and cerebral arteries within the first 72 h; 2) Transthoracic echocardiography (TTE) or Transesophageal echocardiography (TEE) 3) 24-HM; 4) Repeating CT after 24h from the first or, in selected cases, MRI.

All the exams were analysed by a trained neurologist exception made for the 24h-HM which were reviewed by a cardiologist. Thus IS was diagnosed based on the CT performed on patients presenting with clinical signs and symptoms of an acute IS which showed an ischemic brain lesion corresponding to the patient's symptoms (figure 2).

CIS was defined following the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification [27]. We defined AF as an irregular ventricular response in the absence of P-waves, for at least a period of 30 s duration, without a pattern more consistent with an alternative diagnosis[18].

We included in this study: patients aged between 18 years old and 50 years old with an acute brain infarction from cryptogenic origin. Exclusion criteria were not having: an admission EKG, a 24h-HM and a TTE or TEE after the diagnose of CIS.

Stroke severity was evaluated by an accredited neurologist using the National Institute of Health Stroke Scale (NIHSS).

Data analysis

Data analysis was performed with IBM SPSS Statistics 21 program for Microsoft Windows. Continuous variables are described by mean Standard Deviation SD or median [interquartile range (IQR)]. Categorical variables are described by percentages and absolute numbers. The given confidence intervals (CI) are of ninety-five for the prevalence of AF. Univariate analysis was performed with the chi-squared test or Fisher's exact test for dichotomous variables. Continuous variables were analyzed with the t-test or the Mann–Whitney test when appropriate. Values of $P < 0.05$ were considered significant.

We used Meta-Analyst[17] (Center for Evidence-based Medicine, Brown University School of Public Health, Providence, United States) software for statistical analysis and to derive forest plots presenting the results of individual studies and pooled analysis.

Ethic

This study was approved by the Santa Maria Hospital's Ethics Committee.

RESULTS

Observational Study

Among 102 patients diagnosed with ischemic stroke, only 33 had an unknown cause for their stroke and met the inclusion criteria (*Table 2*), with a median age of 46 years old (the younger was 18 years old and the older 50 years old), the median admittance National Institutes of Health Stroke Scale (NIHSS) score was 3 and median discharge RANKIN was 1. The highest incidence rate of CIS was among men (54,5%) compared to women (45,5%). Baseline characteristics of these patients are presented in table 3

AF was not diagnosed in any patient (Figure 2).

Meta-analysis

We found 235 studies. In the end 19 studies were eligible for the predetermined criteria (Table 1 and figure 3).

The proportion of AF in young patients presenting with ischemic stroke, from cryptogenic origin, was 0.034% 95CI (0.022-0.045) as exhibited in figure 1. There was a significant heterogeneity among the pooled studies (I^2>50%).

DISCUSSION

The prevalence of AF found in young adults as a cause of cryptogenic stroke was very low, which is consistent with the literature. According to the FAMA study[10] the prevalence of AF increases with age, being higher among elderly Portuguese people.

AF occurs due to abnormalities in the atrial tissue, in the setting of underlying heart disease. [11] AF affects calcium homeostasis by inducing further electrophysiological and structural changes in the atria.[12] This might explain why age is a risk factor for AF, as shown in literature. [4], [28], [21], [29] This was a retrospective study using a small pool of patients; it is not possible to draw conclusions about all the Portuguese habitants.

This is one of a few studies that specifically analysed the prevalence of AF in young stroke patients, up to 50 years old, due to an intensive search for this arrhythmia.

The majority of analysed data from different studies revealed a lack on HM in all patients reported as having IS of unknown origin, this may therefore underestimate the true prevalence of atrial fibrillation as not all patients were submitted to this exam.

The bulk of studies reported a frequency of AF up to 5% (table 1) in this population. Except for a few studies, which were the great contributors for the heterogeneity found in the present meta-analysis (figure 1). The biggest result disparity was reported by Ghandehari K et al. [30] , who found a prevalence of AF in 23% of IS patients aged 15-45 years old, this was due to the reported cases being related with rheumatic valvular disease, an uncommon finding among the studied populations by the other studies´ authors. Daniel Šaňák et. al. [31] showed a low frequency of AF on 24h-HM and on a prolonged EKG-HM (up to 7 days), however they reported an increased prevalence of AF (9,5% in the ischemic stroke patients aged up to 50 years old) for the reason that they prolonged the investigations of AF using an HM up to 3 weeks. D. Prefasi et al.[17] reported AF as an independent factor of stroke severity in patients aged up to 50 years old who suffered from an IS, and showed a prevalence of 8,9%, in their population, most of AF was previously known, and not a *de novo* finding.

Few studies described in detail the search of AF in young stroke patients, and only ours and Daniel Šaňák´s et. al. [31] performed a 24h-HM to all the included subjects.

After a careful analysis of the data from the literature, the great majority of the studies showed a low prevalence of FA among the CIS patients. Since the meta-analysis shows a low overall prevalence we suggest to review the current indication to perform a continuous EKG HM in all patients under 50 years old presenting with a stroke of unknown origin, because AF is a rare diagnosis. Instead, an EKG could be used as an exclusion diagnostic tool of AF due to its simplicity and cheapness. It would be important to study the economic impact on the use of a long-term EKG-HM in this specific population, which might show an urge to revise the recommended guidelines since they are directed to the general population, not taken in consideration the specificities of the younger.

CONCLUSION

The meta-analysis showed a pooled prevalence of atrial fibrillation as a cause of stroke in young adults of 0.034% 95CI (0.022-0.045). These findings are important to reconsider the performance of a 24-h EKG in all young stroke patients.

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ANEXES

TABLES

Table 1 AF detection in ischemic stroke patients from clinical studies′ data

Study	N	Age	HM	Yield of HM to detect AF	AF detected
Ribeiro	33	18-50	100%	0%	0%
D. Prefasi et al.[17]	157	15-50	24.8%	7.7%	8.9%
Daniel Šaňák et. al. [31]	95	≤50	100%	7.6%	9.5%
A. W. M. Janssen et. al.[4]	49	<50	0%	0%	0%
Ghandehari K et al. [30]	124	15-45	20%	NR	23%
Fromm A et al.[32]	100	<50	57%	1.8%	5%
Leys D et al.[29]	287	15-45	24.7%	NR	4.5%
Spengos K et al.[20]	245	≤45	4.89%	16.6%	2%
Larrue V et al.[9]	318	16-54	15.4%	5.1%[a]	1.26%
Marinin et al.	NR	<50	NR	NR	4.4%
Putaala J et al.[26]	1008	15-49	NR	NR	4.2%
Dharmasaroja PA et al.[7]	99	16-50	NR	NR	4%
Gattellari et al.[33]	1466	18-49	NR	NR	3.95%
Jørgensen HS et al.[4]	50	<50	NR	NR	2%
Lee TH et al.[34]	264	18-45	NR	NR	1.89%
Carolei A et al.[14]	333	≤45	NR	NR	1.8%
Kittner SJ et al.[35]	428	15-44	NR	NR	0.93%
Kristensen et al.[36]	107	18-44	NR	NR	0%
Cerrato P et al.[3]	273	16-49	0	NP	0.73%
Nedeltchev K et al.[37]	203	16-45	NR	NR	0.49%

Abbreviations: *AF*: Atrial Fibrilation; *HM:* Holter Monitoring; *NP:* Not Performed*; NR:* No reference

Table 2 Investigations

Total Ischemic Stroke Patients from 1/1/2013 until 31/12/2015, aged 18-50 years old	*102*
Total Cryptogenic stroke Patients met the inclusion Criteria	33

Table 3 Baseline characteristics

Baseline characteristics	**Total: 33 patients**
Age	46 (Median)
Sex	45.5% (Female) 54.5% (Male)
Admitance NIHSS	3 (Median)
Discharge RANKIN	1(Median)
Hipertension	42.4% (Frequency: 14)
Diabetes Mellitus	12.1% (Frequency: 4)
Smoker	36.4% (Frequency: 12)
Coronary disease	3% (Frequency: 1)
Dyslipidemia	75.8% (Frequency: 25)

FIGURES

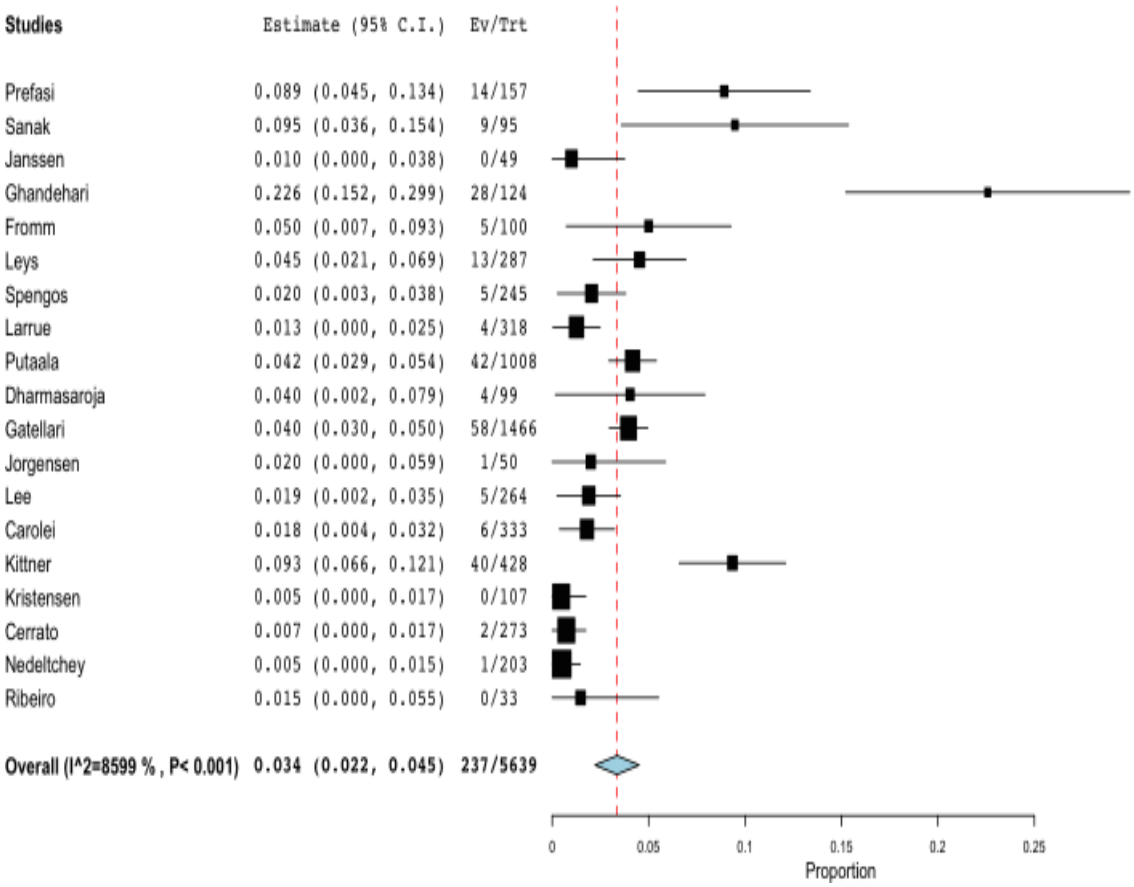

Figure 1 *Forest Plot* of Atrial Fibrillation as a cause of cryptogenic stroke in young adults. The marker size represents the weight of the study.

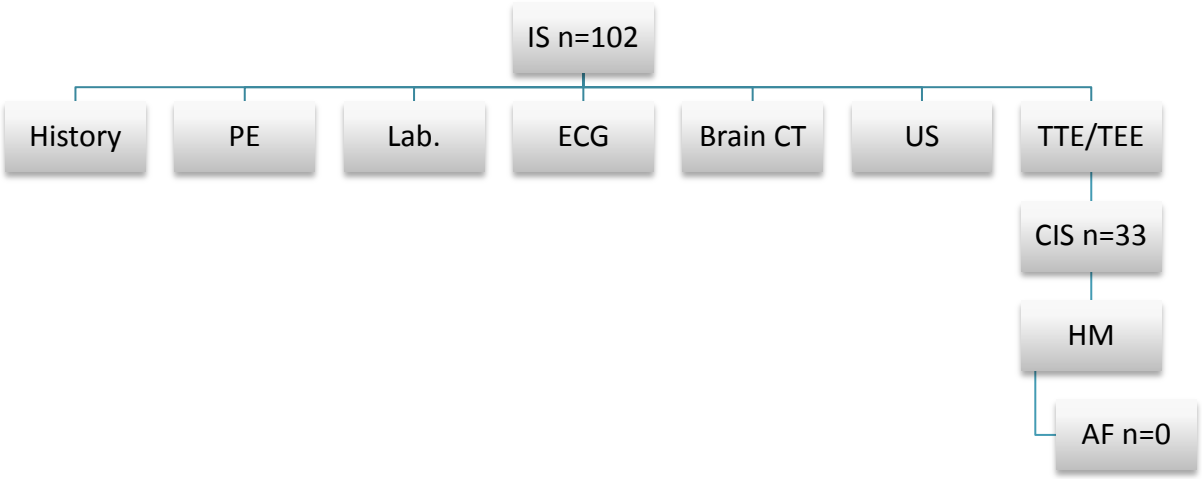

Figure 2 Flow Chart of diagnostic testing for Atrial Fibrillation as a source of cryptogenic Ischemic stroke in patients aged 18 to 50 years old

Abbreviations: *AF*: Atrial Fibrillation *CIS:* Cryptogenic Ischemic Stroke; *CT:* Computed Tomography, which was repeated after 24h from the first; *ECG:* Electrocardiogram; *HM:* 24 hour - Holter Monitoring; *IS:* Ischemic Stroke; *Lab:* laboratory samples containing: hematologic evaluation; biochemistry; syphilis serology; auto-antibodies searched on plasma; pro-thrombotic states; urinalysis *MRI:* Magnetic Resonance Imaging, repeated after 24h from the first CT in selected cases; *PE:* Physical Examination; *TEE:* Transesophageal echocardiography; *TTE:* Transthoracic echocardiography; *US:* Ultrasound of cervical and cerebral arteries within first 72 h; *102*: number of patients diagnosed with Ischemic stroke based on clinical signs and symptoms with a corresponding brain lesion on CT or MRI; *33:* number of patients diagnosed with Cryptogenic Ischemic Stroke following the orientation of the Trial of Org 10172 in Acute Stroke Treatment; *O*: Number of patients detected with Atrial Fibrillation after analysing the ECG and 24h-HM

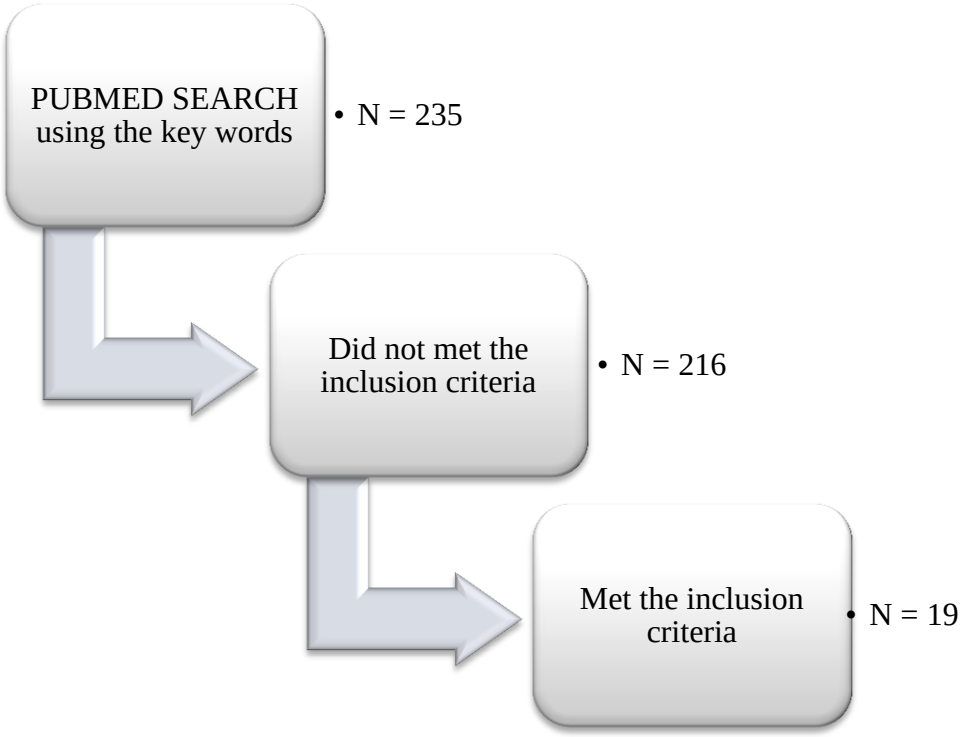

Figure 3: Flow Chart of the study selection

Abbreviations: N – Number of studies; Keywords: stroke AND young AND (atrial fibrillation [Mesh] OR Holter OR electrocardiogram OR arrhythmia)

RESUMO

A Fibrilhação Auricular (FA) é uma causa de acidente vascular cerebral (AVC) é um achado etiológico importante na investigação da causa de acidente vascular cerebral isquémico (AVCI). A investigação da etiologia do AVCI inclui a realização de um eletrocardiograma (ECG) e uma monitorização de 24hora-ECG para deteção de FA em todos os pacientes, independentemente da sua idade. A FA é uma doença mais prevalente em idosos. O objetivo deste trabalho foi estudar a prevalência de FA, como uma causa de AVC, numa amostra da população Portuguesa, com idades entre os 18 a 50 anos, admitidos numa unidade de AVC, e, realizar uma revisão sistemática para estimar a prevalência da FA como causa de AVC nos pacientes jovens.

Realizámos uma análise observacional retrospetiva de centro-único. Todos os dados foram recolhidos da base de dados do departamento de neurologia do Hospital de Santa Maria (HSM) desde 1 de Janeiro de 2013 até 31 de Dezembro de 2015.

A prevalência, de FA, encontrada, foi de zero, com um intervalo de confiança entre 0 e 0,055. Na nossa meta-análise encontrámos uma prevalência da FA, como causa de AVCI nos jovens adultos de 23% a 0%, com a maioria dos estudos a reportar uma prevalência inferior a 5%. Estes achados são importantes, para que se repense no uso 24h-ECG em todos os pacientes jovens.

Palavras-chave: jovens; Fibrilhação; AVC indeterminado; Holter.

O trabalho final exprime a opinião do autor e não da FML.

Índice

INTRODUÇÃO

O AVC é uma causa de morbimortalidade a nível mundial.[1] Os jovens tendem a ter uma menor frequência dos fatores de risco convencionais, diferente dos encontrados nos mais idosos. Nos doentes com mais de 50 anos de idade, as causas *major* de AVC são Fibrilhação Auricular (FA) e doença dos grandes vasos.[2,3] Nos mais jovens, a maioria das causas reportadas são disseção arterial, patência do *foramen ovale*.[4] Um terço dos jovens, que se apresentam com AVCI, a causa permanece indeterminada.[5]

Dados do estudo FAMA, realizado na população Portuguesa, sugerem que a FA como causa de AVC criptogénico (AVCC) em doentes abaixo dos 50 anos de idade tem uma prevalência de 0,2% [6]. Apesar disto, a FA é uma arritmia comum, com uma prevalência estimada de seis milhões na Europa, aumentando em 5 vezes o risco de AVC e é responsável por um em cinco AVCI, sendo geralmente fatais, e, os sobreviventes têm mais sequelas e com maior risco de desenvolver novo AVC. A probabilidade de ter FA aumenta com a idade.[7]

Tanto a Organização Europeia como a American Heart Association /American Stroke Association, nas suas *guidelines*, recomendam a realização de um ECG e pelo menos uma monitorização Holter das 24h (24h-HM) ou monitorização cardíaca continua, para detetar FA, nos doentes que se apresentem com AVCI.[8,9]

Uma vez que só existe um estudo à cerca deste assunto em Portugal, a nossa hipótese é que a FA *de novo*, detetada por 24h-HM é menos frequente que o esperado, nos doentes jovens com AVCC. O objectivo deste trabalho é analisar a prevalência de FA nos jovens com idades entre 18 e 50 anos de idade.

SUJEITOS E MÉTODOS

Para o teste da nossa hipótese foi feito um estudo observacional retrospectivo de centro único. Analisaram-se os dados de uma série de doentes admitidos na unidade de AVC do Hospital de Santa Maria (Hospital terciário, servindo directamente uma população de mais que 372831 doentes); e, uma revisão sistemática da literatura, usando as palavras de pesquisa: "stroke AND young AND (atrial fibrillation [Mesh] or Holter OR electrocardiograma OR arrythmia);

Selecionaram-se estudos desde 1998 até 2015 (última pesquisa realizada a 1 de Janeiro de 2016).

Os Critérios de inclusão foram:

- Estudos observacionais em sujeitos com idades inferiores a 50 anos com AVCC, nos quais foi realizado um ECG.
- Artigos escritos nas línguas: Portuguesa, Inglesa, Francesa, Espanhola; Italiana.

Os critérios de exclusão foram:

- Caso-controlo; Opinião de autor; Estudos de caso; experiências clínicas; comentários clínicos; cartas; notícias do editor.

Para a realização do estudo observacional, foram analisados dados da base do Departamento de Neurologia do Hospital de Santa Maria (Lisboa). Incluíram-se doentes entre os 18 e 50 anos, admitidos na Urgência para o Departamento de Neurologia desde 1 de Janeiro a 31 de Dezembro de 2015, com AVCC, aos quais foi realizado, pelo menos um 24h-HM para detetar FA. A figura 2 mostra a marcha diagnostica.

AVCC foi definido pelo *Trial of Org 10172* no Tratamento Agudo do AVC (TOAST) e a gravidade do AVC avaliada pela Escala do Instituto de saúde de AVC (NIHSS).

O presente estudo foi aprovado pelo Comité de Ética do Hospital de Santa Maria.

ANÁLISE DE RESULTADOS

Os dados foram tratados usando o programa IBM SPSS Statistics 21 para Microsoft Windows, consideraram-se como estatisticamente significativos, os valores de $P < 0.05$. Para a meta-análise usou-se o programa Meta-Analyst, todas as estimativas, foram consideradas estatisticamente diferentes quando $P < 0.05$.

RESULTADOS

Estudo observacional

De uma base de 102 doentes, apenas 33 cumpriram os critérios de inclusão (tabela 2), com uma idade média de 46 anos, e média NIHSS de 3, nenhum apresentou FA. A incidência de AVCC foi detetada nos homens (54,5%). Características iniciais dos doentes estão representadas na tabela 3.

Meta-analise

Dos 235 artigos encontrados, apenas 19 foram elegíveis (tabela 1 e figura 3). Tendo-se verificada uma proporção de 0,034% 95 Intervalo de Confiança (IC) (0,022 –

0,045) como demonstrado na figura 1. Com uma heterogeneidade significativa entre os estudos (I^2 superior a 50%)

DISCUSSÃO

Foi encontrada uma baixa prevalência de FA na maioria dos estudos, indo de encontro aos nossos resultados.

A maioria dos estudos reporta uma prevalência de FA de até 5% (tabela 1) Com exceção de alguns estudos, que contribuem para a heterogeneidade dos resultados obtidos pela meta-analise.

CONCLUSÃO

Dada a baixa prevalência de FA como causa de AVCI nos jovens, propomos uma revisão das indicações para o uso indiscriminado de 24h-HM.

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ANEXOS

TABELAS

Tabela 1 FA detetada na bibliografia, em doentes com AVCI

Study	N	Idade	HM	Realização de HM para detetar FA	FA detada
Ribeiro	33	18-50	100%	0%	0%
D. Prefasi et al.[10]	157	15-50	24.8%	7.7%	8.9%
Daniel Šaňák et. al. [11]	95	≤50	100%	7.6%	9.5%
A. W. M. Janssen et. al.[3]	49	<50	0%	0%	0%
Ghandehari K et al. [12]	124	15-45	20%	SR	23%
Fromm A et al.[13]	100	<50	57%	1.8%	5%
Leys D et al.[14]	287	15-45	24.7%	SR	4.5%
Spengos K et al.[15]	245	≤45	4.89%	16.6%	2%
Larrue V et al.[16]	318	16-54	15.4%	5.1%[a]	1.26%
Marinin et al.	NR	<50	NR	SR	4.4%
Putaala J et al.[17]	1008	15-49	NR	SR	4.2%
Dharmasaroja PA et al.[18]	99	16-50	NR	SR	4%
Gattellari et al.[19]	1466	18-49	NR	SR	3.95%
Jørgensen HS et al.[3]	50	<50	NR	SR	2%
Lee TH et al.[20]	264	18-45	NR	SR	1.89%
Carolei A et al.[5]	333	≤45	NR	SR	1.8%
Kittner SJ et al.[21]	428	15-44	NR	SR	0.93%
Kristensen et al.[22]	107	18-44	NR	SR	0%
Cerrato P et al.[4]	273	16-49	0	NE	0.73%
Nedeltchev K et al.[23]	203	16-45	NR	SR	0.49%

Abbreviations: FA: Fibrilhação Auricular; *HM:* Monitorização Holter ; *NE:* Não Efetuado*; SR:* Sem referencia

Tabela 2 Investigações

Total de doentes com AVCI de 1/1/2013 até 31/12/2015, com idades de 18-50 anos	*102*
Total de doentes com AVCC que cumpriram os critérios de inclusão.	33

Tabla 3 Características Basais

Características Basais	Total: 33 patientes
Idade	46 (Media)
Sexo	45,5% (Mulher) 54,5% (Homem)
NIHSS à admissão	3 (Media)
RANKIN na alta	1(Media)
Hipertensão	42,4% (Frequência: 14)
Diabetes Mellitus	12,1% (Frequência: 4)
Fumador	36,4% (Frequência: 12)
Doença Coronária	3% (Frequência: 1)
Dislipidémia	75,8% (Frequência: 25)

FIGURAS

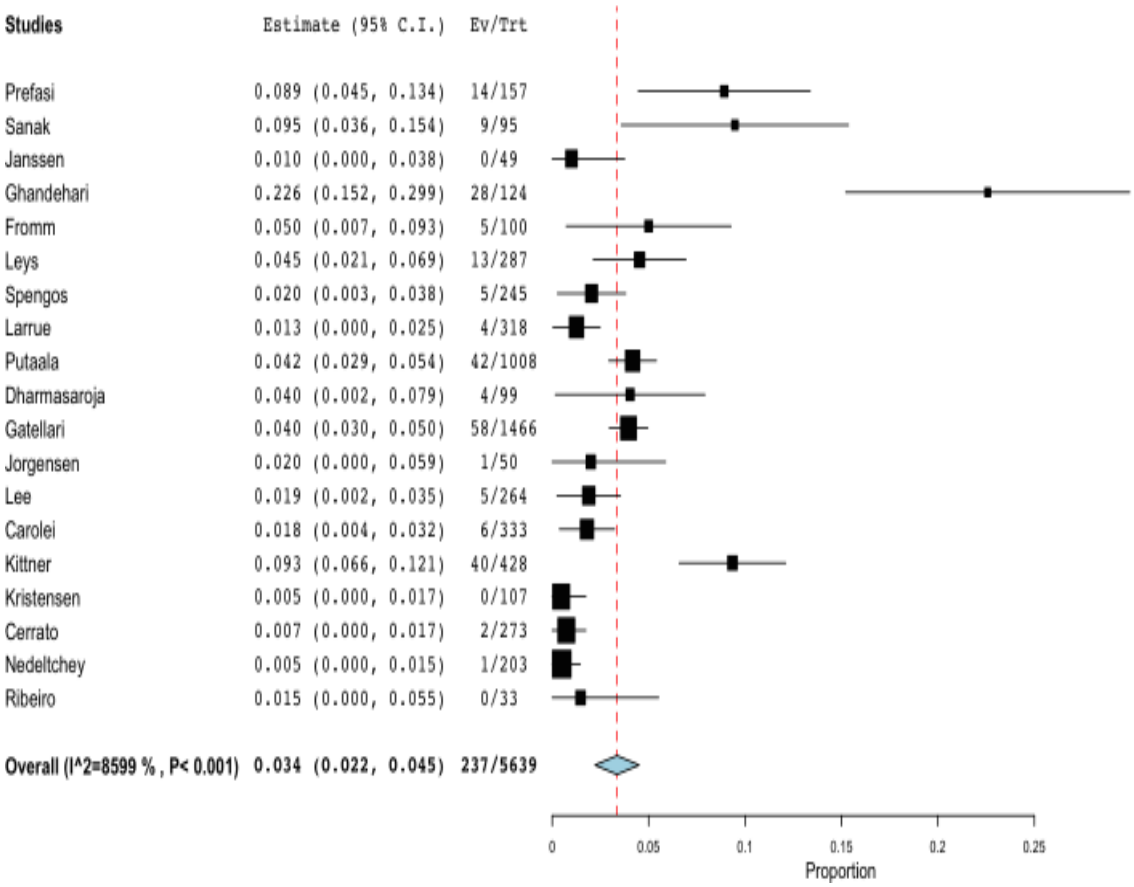

Figura 3 *Forest Plot* da Fibrilhação auricular como causa de AVCC em adultos jovens . O tamanho da marca, representa a prevalência agrupada do estudo.

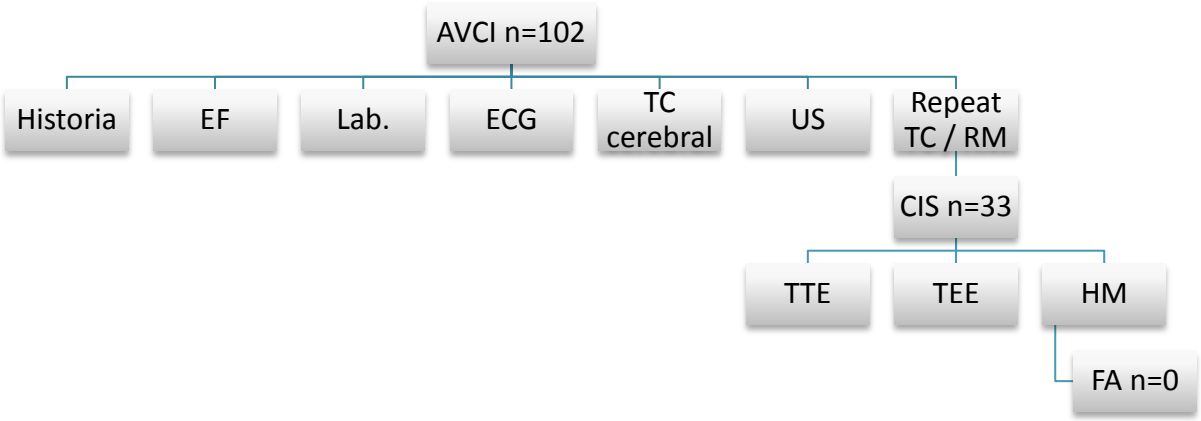

Figura 4 Realização de Testes diagnostic para a Fibrilhação auricular, como fonte de Acidente Vascular Cerebral Isquémco de origem Criptogénica em jovens adultos, com idades entre 18 e 50 anos.

Abreviaturas: *AVCI:* Acidente vascular isquémico. *CIS:* *Acidente vascular isquémico de origem criptogénica*. *ECG:* Electrocardiogram. *EF:* Exame Físico. *ETE:* Ecocardiografia transesofágica. *ETT:* Ecocardiografia Transtoracica. *FA:* Fibrilhação Auricular. *HM:* Monitorizaçã Holter das 24h. *Lab:* Análises de sangue: avaliação hematológica; bioquímica; serologias para sífilis; auto-anticorpos; estados protromboticos; análise de urina. *MRI:* Magnetic Resonance Imaging, repeated after 24h from the first CT in selected cases. *TC:* Tomografia Computorizada, a qual foi repetida depois de 24h da primeira. *US:* Ecografia das arterias cerebrais e arteriais nas primeiras 72 horas. *102:* numero de pacientes com diagnostic de AVC Isquémico com base nos sinais e sintomas clínicos, com uma lesão cerebral correspondente na TC ou RM. *33:* numero de pacientes diagnosticados com CIS de acordo com as orientações do Trial of Org 10172 in Acute Stroke Treatment. *O*: Numero de pacientes com FA, após a análise de ECH e do 24h-HM.